

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTELLAS US LLC,)	
ASTELLAS PHARMA US, INC.)	
and GILEAD SCIENCES, INC.,)	
)	
Plaintiffs,)	
)	C.A. No. 18-01675-CFC
v.)	
)	(CONSOLIDATED)
APOTEX INC.,)	
)	
Defendant.)	

FIRST AMENDED COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs Astellas US LLC and Astellas Pharma US, Inc. (collectively, “Astellas”) and Gilead Sciences, Inc. (“Gilead”) (Astellas and Gilead, collectively, “Plaintiffs”), by their attorneys, hereby allege as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement arising under the patent laws of the United States, Title 35, United States Code, against Defendant Apotex Inc. (“Apotex”). This action relates to Abbreviated New Drug Application (“ANDA”) No. 207604 filed by Apotex with the U.S. Food and Drug Administration (“FDA”).

2. In ANDA No. 207604, Apotex seeks approval to market 0.4 mg/5 mL (0.08 mg/mL) intravenous solution of regadenoson, a generic version of Plaintiffs’ Lexiscan® drug product (the “Apotex ANDA product”), prior to expiration of U.S. Patent Nos. 8,106,183 (the “’183 patent”), RE 47,301 (the “’301 patent”), and 8,524,883 (the “’883 patent”). The ’183 patent, ’301 patent, and ’883 patent are collectively referred to herein as the “patents-in-suit.”

PARTIES

3. Astellas US LLC is a limited liability company organized and existing under the laws of the State of Delaware having its principal place of business at 1 Astellas Way, Northbrook, Illinois 60062.

4. Astellas Pharma US, Inc. is a corporation organized and existing under the laws of Delaware, having its principal place of business at 1 Astellas Way, Northbrook, IL 60062.

5. Gilead is a corporation organized and existing under the laws of Delaware, having its principal place of business at 333 Lakeside Drive, Foster City, CA 94404.

6. Plaintiffs are engaged in the business of creating, developing, and bringing to market revolutionary pharmaceutical products to help patients prevail against serious diseases, including diagnostic pharmacologic stress agents. Plaintiffs sell Lexiscan in this judicial district and throughout the United States.

7. Upon information and belief, Apotex is a corporation organized and existing under the laws of Canada, having its principal place of business at 150 Signet Drive, Toronto, Ontario, M9L 1T9, Canada.

JURISDICTION AND VENUE

8. This case arises under the patent laws of the United States, 35 U.S.C. §§ 100, *et seq.*, and this Court has jurisdiction over its subject matter under 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

9. This Court has jurisdiction over Apotex because, *inter alia*, Apotex has committed an act of patent infringement under 35 U.S.C. § 271(e)(2) and intends a future course of conduct that includes acts of patent infringement in Delaware. These acts have led and will lead to

foreseeable harm and injury to Plaintiffs, both Delaware corporations, in Delaware. For example, on information and belief, following approval of ANDA No. 207604, Apotex will make, use, import, sell, and/or offer for sale the Apotex ANDA Product in the United States, including in Delaware, prior to the expiration of the patents-in-suit.

10. This Court also has jurisdiction over Apotex because, *inter alia*, this action arises from actions of Apotex directed toward Delaware, and because Apotex has purposefully availed itself of the rights and benefits of Delaware law by engaging in systematic and continuous contacts with Delaware. Upon information and belief, Apotex regularly and continuously transacts business within Delaware, including by selling pharmaceutical products in Delaware either directly or indirectly through affiliated companies, including Apotex Corp. Upon information and belief, Apotex derives substantial revenue from the sale of those products in Delaware and has availed itself of the privilege of conducting business within Delaware.

11. Apotex has previously consented to suit in this judicial district and has availed itself of Delaware courts through the assertion of counterclaims in suits brought in Delaware including *Warner Chilcott Co. v. Apotex Inc.*, C.A. No. 10-1111-LPS, D.I. 8 (D. Del. Jan. 31, 2011); *Pfizer Inc. v. Apotex, Inc.*, C.A. No. 11-606-GMS, D.I. 10 (D. Del. Oct. 3, 2011); *Senju Pharm. Co. v. Apotex Inc.*, C.A. No. 12-0159-SLR, D.I. 9 (D. Del. Mar. 16, 2012); *Alcon Pharm. v. Apotex Inc.*, C.A. No. 12-960-SLR, D.I. 6 (D. Del. July 23, 2012); *Pfizer Inc. v. Apotex Inc.*, C.A. No. 12-809-SLR, D.I. 18 (D. Del. Aug. 27, 2012); *UCB Inc. v. Apotex Corp.*, C.A. No. 13-1209-LPS, D.I. 12 (D. Del. Sept. 9, 2013); *Pfizer Inc. v. Apotex Inc.*, C.A. No. 13-1613-SLR, D.I. 8 (D. Del. Oct. 17, 2013); *Meda Pharm., Inc. v. Apotex Inc.*, C.A. No. 14-1453-LPS, D.I. 93 (D. Del. Mar. 9, 2016);

Salix Pharm., Inc. v. Apotex Inc., C.A. No. 15-880-GMS, D.I. 15 (D. Del. Mar. 14, 2016); *Bristol-Myers Squibb Co. v. Apotex Inc.*, C.A. No. 17-399-LPS, D.I. 8 (D. Del. May 4, 2017).

12. In the alternative, this Court has jurisdiction over Apotex because the requirements of Federal Rule of Civil Procedure 4(k)(2)(A) are met.

13. Venue is proper in this Court as to each claim against Apotex under 28 U.S.C. § 1391(c)(3), because Apotex, upon information and belief, is not a resident of the United States and may thus be sued in any judicial district.

14. For these reasons, and for other reasons that will be presented to the Court if jurisdiction and/or venue are challenged, the Court has personal jurisdiction over Apotex, and venue in this judicial district is proper.

PATENTS-IN-SUIT

15. On January 31, 2012, the U.S. Patent and Trademark Office duly and legally issued the '183 patent, titled "Process for preparing an A_{2A}-adenosine receptor agonist and its polymorphs." A true and correct copy of the '183 patent is attached hereto as Exhibit A. The claims of the '183 patent are valid, enforceable, and not expired. Gilead is the owner of the '183 patent and Astellas US LLC is the exclusive licensee of the '183 patent.

16. On March 19, 2019, the United States Patent and Trademark Office duly and legally issued the '301 patent, titled "Process for preparing an A_{2A}-adenosine receptor agonist and its polymorphs." The '301 patent is a reissue of U.S. Patent No. 9,085,601 (the "'601 patent"), which issued on July 21, 2015. A true and correct copy of the '301 patent is attached hereto as Exhibit B. The claims of the '301 patent are valid, enforceable, and not expired. Gilead is the owner of the '301 patent and Astellas US LLC is the exclusive licensee of the '301 patent.

17. On September 3, 2013, the United States Patent and Trademark Office duly and legally issued the '883 patent, titled "Monohydrate of (1-{9-[4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-6-aminopurine-2-yl}pyrazol-4-yl)-N-methylcarboxamide." A true and correct copy of the '883 patent is attached hereto as Exhibit C. The claims of the '883 patent are valid, enforceable, and not expired. Gilead is the owner of the '883 patent and Astellas US LLC is the exclusive licensee of the '883 patent.

18. On October 23, 2018, Apotex filed a Complaint for Declaratory Judgment that the claims of the '183 patent and the '601 patent (later reissued as the '301 patent) are not infringed in the Northern District of California ("California action"). *See Apotex Inc. v. Gilead Scis., Inc. and Astellas Pharma US, Inc.*, C.A. No. 18-6475-JSC, D.I. 1 (N.D. Cal. Oct. 23, 2018). Plaintiffs moved to dismiss the California action on the grounds that jurisdiction and venue in that forum are improper on November 30, 2018. The Northern District of California dismissed the claims in the California action on January 31, 2019. Apotex filed a motion for leave to file a motion for reconsideration of the dismissal order on February 20, 2019, which is currently pending before the Court.

19. On October 25, 2018, Plaintiffs filed a Complaint against Apotex for the infringement of the '183 and '601 patents in the District of Delaware. In the Complaint, Plaintiffs noted that "[t]he '601 patent is the subject of a pending reissue proceeding (Reissue Application No. 15/653,860)." The '601 patent reissued as the '301 patent on March 19, 2019. Upon issuance of the '301 patent, the '601 patent was surrendered to the Patent Office.

20. Shortly following the '301 patent's issuance, and at Astellas' request, the FDA added the '301 patent to and de-listed the '601 patent from the FDA Orange Book for Lexiscan®

in early April 2019. Plaintiffs then promptly contacted all defendants in this consolidated action, including Apotex, and proposed amending the Complaint to replace the '601 patent with the reissued '301 patent, providing a proposed stipulation to that effect on April 11, 2019. Having received no response from Apotex on Plaintiffs' proposal, Plaintiffs again contacted Apotex on May 1, 2019, requesting Apotex's position on amending the Complaint to replace the '601 patent with the '301 patent, as well as Plaintiffs' proposed amendment of the Complaint to additionally assert the '883 patent. On May 6, 2019 and May 16, 2019, the Parties met and conferred regarding addition of the '301 patent and the '883 patent to the case. Apotex never disputed the fact that the '301 patent should be part of the case, or that the '601 patent should not be.

21. Apotex did not answer Plaintiffs' original Complaint. Instead, Apotex moved to dismiss the Complaint, and Plaintiffs are thus amending as of right pursuant to Federal Rule of Civil Procedure 15(a)(1)(B).

22. Astellas Pharma US, Inc. is the holder of New Drug Application ("NDA") No. 022161, by which the FDA granted approval for the marketing and sale of 0.4 mg/5 mL (0.08 mg/mL) intravenous solution of regadenoson. Plaintiffs market 0.4 mg/5 mL (0.08 mg/mL) intravenous solution of regadenoson in the United States, under the trade name "Lexiscan®." The FDA's official publication of approved drugs (the "Orange Book") includes Lexiscan together with the '183 and '301 patents. Lexiscan is a pharmacologic agent used in a cardiac nuclear stress test. Lexiscan works by increasing blood flow in the coronary arteries. Lexiscan is given prior to a myocardial perfusion imaging (MPI) test, which provides physicians with detailed information about blood flow into a patient's heart. Approximately half of the people undergoing a cardiac stress test are unable to use a treadmill or a stationary bicycle because of medical conditions.

Lexiscan may be used when a person is unable to exercise enough to increase blood flow to the heart during a cardiac nuclear stress test.

23. The prescribing information for Lexiscan identifies the drug as “a pharmacologic stress agent indicated for radionuclide myocardial perfusion imaging (MPI) in patients unable to undergo adequate exercise stress.” A copy of the complete prescribing information for Lexiscan approved in NDA No. 022161 is attached as Exhibit D.

24. The '883 patent claims processes for preparing a pharmaceutical composition of regadenoson with at least one pharmaceutically acceptable carrier.

INFRINGEMENT BY APOTEX

25. By letters dated December 10, 2014; October 15, 2015; August 24, 2018; and August 31, 2018, Apotex notified Plaintiffs that Apotex had submitted ANDA No. 207604 to the FDA under Section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355(j)) (“the Lexiscan Notice Letters”).

26. The Lexiscan Notice Letters state that Apotex has submitted an ANDA under 21 U.S.C. § 355(j) to engage in the commercial manufacture, use, importation, offer for sale, or sale of the Apotex ANDA product before the expiration of the '183 and '601 patents. Upon information and belief, Apotex intends to—directly or indirectly—engage in the commercial manufacture, use, and sale of the Apotex ANDA product.

27. By filing ANDA No. 207604, Apotex has necessarily represented to the FDA that the Apotex ANDA product has the same active ingredient as Lexiscan, has the same dosage form and strength as Lexiscan, and is bioequivalent to Lexiscan.

28. Upon information and belief, Apotex is seeking approval to market the Apotex ANDA product for the same approved indication as Lexiscan.

29. In the Lexiscan Notice Letters, Apotex stated that the '183 and '601 patents are invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, and sale of the Apotex ANDA product.

30. In the Lexiscan Notice Letters, Apotex offered confidential access to portions of its ANDA No. 207604, on terms and conditions set forth in the Lexiscan Notice Letters ("the Apotex Offer"). Apotex requested that Plaintiffs accept the Apotex Offer before receiving access to Apotex's ANDA No. 207604. The Apotex Offer contained unreasonable restrictions well beyond those that would apply under a protective order on who could view the ANDA. For example, the Apotex Offer contained a broad patent prosecution bar, which, among other things, does not have a carve out for *inter partes* reviews or other adversarial proceedings, and a broad bar on any work related to actions before the FDA. The Apotex Offer unreasonably restricted the ability of counsel to seek the opinions of Plaintiffs' employees and outside experts. The restrictions Apotex has placed on access to ANDA No. 207604 contravene 21 U.S.C. § 355(j)(5)(C)(i)(III), which states that an offer of confidential access "shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, ***as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information***" (emphasis added).

31. Upon information and belief, Apotex uses processes covered by the claims of the '883 patent to prepare Apotex's ANDA product.

32. Upon information and belief, the product resulting from the process claimed in the '883 patent is made, used, offered for sale, and/or sold without material change to the product resulting from the process claimed by the '883 patent.

33. The product resulting from the process claimed by the '883 patent is not a nonessential and/or trivial component of another product.

34. Upon information and belief, Apotex intends to import into the United States and/or offer to sell, sell, make, and/or use within the United States the Apotex ANDA product, which is made by the process patented by the '883 patent, prior to the expiration of the '883 patent.

35. Upon information and belief, Apotex has made and will continue to make substantial and meaningful preparations to practice the method claimed in the '883 patent and/or import, offer to sell, sell, make, and/or use within the United States its ANDA product, which is made by the process covered by the '883 patent, prior to the expiration of the '883 patent. Apotex's preparations include, but are not limited to, developing Apotex's generic product, filing ANDA No. 207604, and engaging in litigation concerning the Apotex ANDA product.

36. Upon information and belief, Apotex plans to continue to use the processes claimed in the '883 patent to make its ANDA product.

37. Upon information and belief, Apotex had actual and/or constructive notice of the '883 patent prior to filing ANDA No. 207604.

COUNT I

(INFRINGEMENT OF THE '183 PATENT)

38. Each of the preceding paragraphs 1 to 37 is incorporated as if fully set forth herein.

39. Apotex's submission of ANDA No. 207604 to obtain approval to engage in the commercial manufacture, use, offer to sell, or sale of the Apotex ANDA product prior to the expiration of the '183 patent constituted a technical act of infringement of at least one of the claims of the '183 patent, either literally or under the doctrine of equivalents, including but not limited to claims 1-3 and 8-9, under 35 U.S.C. § 271(e)(2)(A).

40. Apotex's commercial manufacture, use, offer to sell, sale, or importation of the Apotex ANDA product prior to the expiration of the '183 patent, and its inducement of and/or contribution to such conduct, would further infringe at least one of the claims of the '183 patent, either literally or under the doctrine of equivalents, including at least claims 1-3 and 8-9, under 35 U.S.C. § 271(a), (b), (c) and/or (g).

41. Upon FDA approval of Apotex's ANDA No. 207604, Apotex will infringe one or more claims of the '183 patent, either literally or under the doctrine of equivalents, including at least claims 1-3 and 8-9, by making, using, offering to sell, and selling the Apotex ANDA product in the United States and/or importing said product into the United States, and/or by actively inducing and contributing to infringement of the '183 patent by others, under 35 U.S.C. § 271(a), (b), (c) and/or (g), unless enjoined by the Court.

42. If Apotex's marketing and sale of the Apotex ANDA product prior to expiration of the '183 patent and all other relevant exclusivities are not enjoined, Plaintiffs will suffer substantial and irreparable harm for which there is no remedy at law.

COUNT II

(INFRINGEMENT OF THE '301 PATENT)

43. Each of the preceding paragraphs 1 to 42 is incorporated as if fully set forth herein.

44. Apotex's submission of ANDA No. 207604 to obtain approval to engage in the commercial manufacture, use, offer to sell, or sale of the Apotex ANDA product prior to the expiration of the '301 patent constituted a technical act of infringement of at least one of the claims of the '301 patent, either literally or under the doctrine of equivalents, including but not limited to claims 6, 11, and 17, under 35 U.S.C. § 271(e)(2)(A).

45. Apotex's commercial manufacture, use, offer to sell, sale, or importation of the Apotex ANDA product prior to the expiration of the '301 patent, and its inducement of and/or contribution to such conduct, would further infringe at least one of the claims of the '301 patent, either literally or under the doctrine of equivalents, including but not limited to claims 6, 11, and 17, under 35 U.S.C. § 271(a), (b), (c) and/or (g).

46. Upon FDA approval of Apotex's ANDA No. 207604, Apotex will infringe one or more claims of the '301 patent, either literally or under the doctrine of equivalents, including but not limited to claims 6, 11, and 17, by making, using, offering to sell, and selling the Apotex ANDA product in the United States and/or importing said product into the United States, and/or by actively inducing and contributing to infringement of the '301 patent by others, under 35 U.S.C. § 271(a), (b), (c) and/or (g), unless enjoined by the Court.

47. If Apotex's marketing and sale of the Apotex ANDA product prior to expiration of the '301 patent and all other relevant exclusivities are not enjoined, Plaintiffs will suffer substantial and irreparable harm for which there is no remedy at law.

COUNT III

(DECLARATORY JUDGMENT OF INFRINGEMENT OF THE '883 PATENT)

48. Each of the preceding paragraphs 1 to 47 is incorporated as if fully set forth herein.

49. A definite and concrete, real and substantial, justiciable controversy of sufficient immediacy and reality exist between Plaintiffs and Apotex regarding infringement of the '883 patent.

50. Apotex has made and will continue to make substantial and meaningful preparations to perform the processes claimed in the '883 patent or to import a product which is made by a process claimed by the '883 patent into the United States prior to the expiration of the '883 patent.

51. Apotex's conduct including, but not limited to, the filing of ANDA No. 207604, attempting to meet the regulatory requirements for approval of ANDA No. 207604, and engaging in litigation concerning the Apotex ANDA product demonstrate a refusal to change its course of action.

52. Apotex's performance of the processes claimed in the '883 patent and/or importation in the United States, offers to sell, sale, and/or use of Apotex's products made by the patented process prior to the expiration of the '883 patent, and its inducement of and/or contribution to such conduct, would infringe claims 1-5, of the '883 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(a), (b), (c) and/or (g).

53. Plaintiffs should be granted a judicial declaration that the importation into the United States, use, offer for sale, and/or sale in the United States of a product made using the processes claimed in the '883 patent, the use of the processes claimed in the '883 patent, and/or actively inducing and contributing to infringement of the '883 patent by others will constitute infringement of the '883 patent under 35 U.S.C. § 271 (a), (b), (c) and/or (g).

54. If Apotex's marketing and sale of the Apotex ANDA product prior to expiration of the '883 patent and all other relevant exclusivities are not enjoined, Plaintiffs will suffer substantial and irreparable harm for which there is no remedy at law.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs pray that this Court grant the following relief:

1. A judgment that the claims of the '183 and '301 patents are not invalid, are not unenforceable, and are infringed by Apotex's submission of ANDA No. 207604, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(e)(2)(A), and that Apotex's making, using, offering to sell, or selling in the United States, or importing into the United States the Apotex ANDA product will infringe the claims of the '183 and '301 patents, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(a), (b), (c) and/or (g).

2. An order pursuant to 35 U.S.C. § 271(e)(4)(A) providing that the effective date of any approval of ANDA No. 207604 shall be a date which is not earlier than the latest expiration date of the '183 and '301 patents, including any extensions and/or additional periods of exclusivity to which Plaintiffs are or become entitled.

3. A judgment declaring that Apotex's importing, selling, offering to sell, and/or using the generic product described in ANDA No. 207604, or inducing or contributing to such conduct, will infringe the '883 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. §271(a), (b), (c) and/or (g);

4. An order permanently enjoining Apotex, its affiliates, subsidiaries, and each of its officers, agents, servants and employees and those acting in privity or concert with them, from making, using, offering to sell, or selling in the United States, or importing into the United States

the Apotex ANDA product until after the latest expiration date of the patents-in-suit, including any extensions and/or additional periods of exclusivity to which Plaintiffs are or become entitled.

5. Damages or other monetary relief, including costs, fees, pre- and post-judgment interest, to Plaintiffs if Apotex engages in commercial manufacture, use, offers to sell, sale, or importation in or into the United States of the Apotex ANDA product prior to the latest expiration date of the patents-in-suit, including any extensions and/or additional periods of exclusivity to which Plaintiffs are or become entitled.

6. Such further and other relief as this Court deems proper and just, including any appropriate relief under 35 U.S.C. § 285.

Dated: June 7, 2019

FISH & RICHARDSON P.C.

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